Prediction of future cognitive scores and dementia onset in Mild Cognitive Impairment patients

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Introduction

Alzheimer's disease (AD) is characterized by changes in brain structure and cognition that can be observed in subjects with a Mild Cognitive Impairment (MCI). MCI subjects can evolve to develop AD or not, and identifying those who will is a key challenge (Falahati et al. 2014; Arbabshirani et al. 2017). Most approaches have focused on predicting a future AD diagnosis (Moradi et al. 2015; Ramírez et al. 2017). On the other hand, we believe that predicting the future cognitive scores would provide a more comprehensive view of the future patient state to the clinician, and thus result in more interpretable decision support systems. We therefore propose a method for identifying MCI subjects who will progress to AD within 1 year by first predicting the evolution of their cognitive scores, and then predicting a diagnosis from the predicted scores.

Methods

Our method is composed of two steps (Figure 1). In a first step, we use a linear regression to predict the future of cognitive scores (ADAS, MMSE, RAVLT and CDR) at time t + 1 year using MRI extracted volumes (whole brain, entorhinal, fusiform, mid temporal, ventricles and hippocampus volumes), socio-demographic information, APOE genotype and the cognitive scores at time t. In a second step, we use the predicted features to estimate the diagnosis at the same time point (t + 1 year) using a Gaussian kernel Support Vector Machine (SVM).

We consider different approaches to improve this prediction pipeline. We consider using more input features: FDG PET SUVr and detailed MRI features (regional cortical thickness and white matter volumes). We also consider learning the regression on different groups, depending on the age (< 65 years old and > 65 years old), the amyloid status or the APOE genotype.

As our method only uses the latest visit for the prediction, we consider using information from former visits as well in 3 different approaches described in Figure 1: "averaging" (averaging the cognitive score predictions made using different visits), "stacking"

(stacking our cognitive score prediction with the output of a time linear regression) and "rate of change" (including the rate of change of the features in the inputs of the regression).

We evaluate our approach on the MCI patients of the ADNI database, using for each subject the latest pair of visits separated by a 1 year interval. Among the 480 subjects with such a pair and a MCI diagnosis before the latest visit, 15% converted to AD. Performance measures are obtained by splitting the cohort 50 times into a training (70%) and test (30%) set. As a comparison, we predict the diagnosis at time t+1 by using a linear SVM on the features at time t directly.

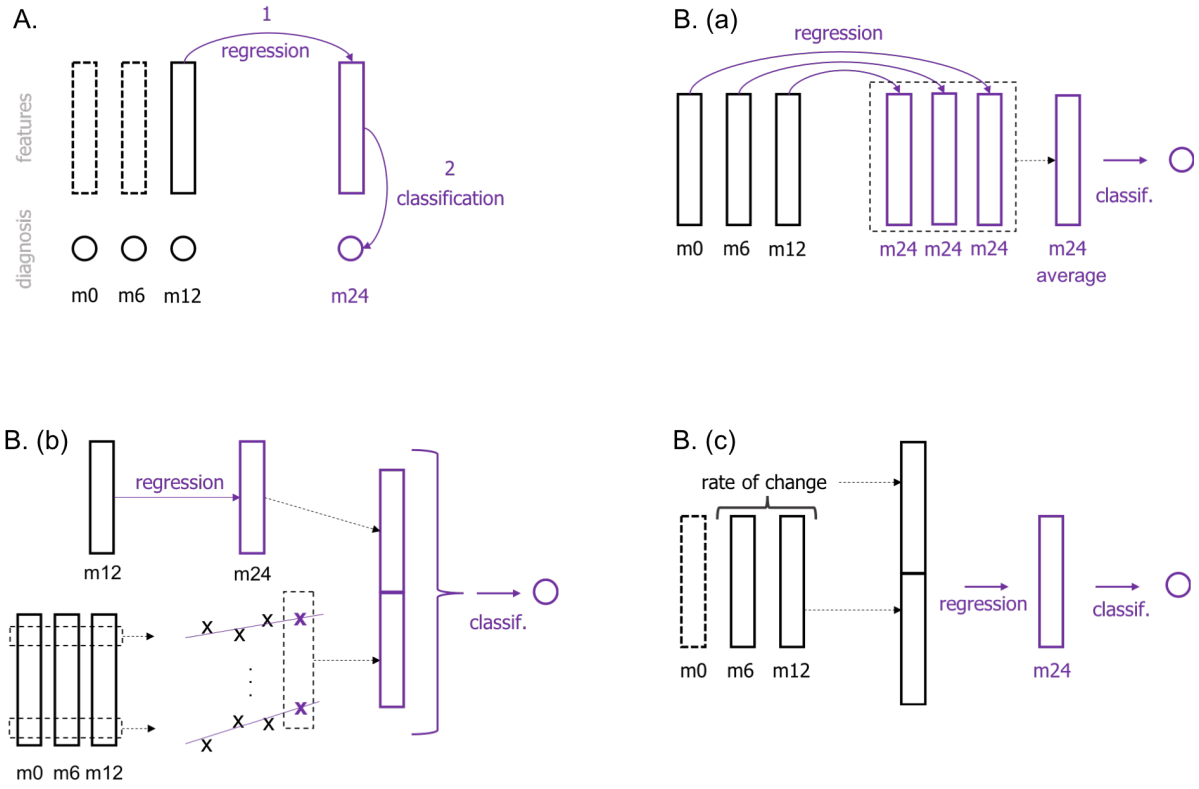

Figure 1. Proposed approaches : A. cross-sectional framework; B. longitudinal framework, with 3 propositions: (a) averaging, (b) stacking, (c) rate of change.

Results

Our method resulted in a Mean Absolute Error (MAE) of 1.51 ± 0.13 on MMSE prediction and of 3.69 ± 0.28 on ADAS prediction. It reached an Area under the ROC curve (AUC) of 87.9 ±2.7, whereas direct classification gave an AUC of 86.6 ±2.2, which is not significantly different. The results did not improve when using more features or building different regression groups (all AUC are presented in Table 1, similar conclusions can be drawn using the MAE). Averaging the predictions from different visits lowered the performance as predicting further in time is harder. The stacking did not improve the results, nor using a rate of change. The best results are therefore achieved using the simplest approach, and are not significantly different from those obtained using direct classification.

			Method	AUC	bacc
			Proposed approach	87.9 ± 2.7	77.1 ± 6.1
extra features			+ FDG PET	86.7 ± 3.1	75.1 ± 3.9
			+ detailed MRI	88.1 ± 2.8	76.9 ± 5.0
	groups	Age		87.7 ± 2.9	74.3 ± 7.2
		Amyloid status		87.5 ± 2.9	74.6 ± 5.8
		APOE genotype		87.4 ± 3.3	77.2 ± 4.1
longitudinal			Averaging	83.3 ±3.9	75.4 ± 5.8
			Stacking	87.6 ±3.3	75.9 ± 5.7
			Rate of change	87.8 ± 3.1	77.9 ± 6.5

Table 1. AUC and balanced accuracy (bacc) obtained on the tested approaches, in the form mean performance ± standard deviation

Conclusions

We proposed to predict the conversion of MCI subjects to AD by first predicting the evolution of cognitive scores. The classification performances are similar to the ones obtained by predicting the future diagnosis from the current features. However, with the prediction of the future cognitive scores, it is possible to understand how the diagnosis prediction was made. We believe that such approaches are more likely to be adopted by the clinicians.

References

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